-- **59.** The antibody of claim 42 which is a polyclonal antibody.

60. The antibody of claim 42 which is a monoclonal antibody.

61. The antibody of claim 43 which is a polyclonal antibody.

62. The antibody of claim 43 which is a monoclonal antibody. --

REMARKS

The amendment to claim 42 adds two SEQ ID NO's which were inadvertently left out of the claim. The amendment does not narrow the scope of the claim; in fact, it broadens it. New claims 59-62 recite embodiments of the claimed invention and are fully supported by the specification.

The priority of the instant application is clarified by the amendment to the specification made herein. The earliest US filing, the '248 application, was made on June 11, 1993, within one year of the filing of the earliest of the two German priority documents (June 11, 1992). Therefore, continuity of the German priority documents and the instant U.S. application is proper.

The Declaration/POA filed with the instant application is proper. It is a copy of the declaration filed in the ancestor application, 08/075,248. The facts that the original filing was accepted by the PTO and that examination ensued prove that the specification was attached.

Corrected drawings will be filed after the application is allowed.

There is no need to deposit the claimed antibodies, at least because, in the words of the Examiner, the antibodies are "readily obtainable by a repeatable method set forth in the specification." Following conventional, art-recognized procedures, the claimed antibodies, *i.e.*, antibodies which exhibit specificity for the recited epitopes (*e.g.*, claim 42) or for p60 from pathogenic listeria (*e.g.*, claim 43), are readily and repeatedly obtainable. Note that the instant claims read on generic polyclonal or monoclonal antibodies; no specific antibody species are recited. For appropriate methods to obtain the claimed antibodies, see, *e.g.*, the specification at page 11, line 20 to page 12, line 31, which presents conventional methods for making polyclonal and monoclonal antibodies, and the copy of one of the references cited in that passage, Harlow and Lane, which is attached hereto. See also Example 11, which describes a method to generate polyclonal antibodies, and Example 12, which describes a method to generate monoclonal antibodies. Methods to confirm the specificity of antibodies

are also conventional, and are discussed in the section of the specification indicated above and further herein below.

The Examiner's allegation that applicants have not proven the instantly claimed antibodies to be specific for p60, or for p60 from pathogenic bacteria, is incorrect. The specification clearly teaches that the claimed antibodies are specific for p60 from pathogenic *Listeria*, *e.g.*, *Listeria monocytogenes*. The fact that the peptide discussed on page 11, lines 5-10, failed to generate an antiserum which reacted with p60 is irrelevant. That peptide was discussed in order to emphasize that one must screen for those peptides which generate specific antibodies. This is routine. The claimed antibodies were, of course, all generated from peptides which do give rise to specific antibodies. It is the Examiner's burden to provide reasons to cast doubt on applicants' assertion that the claimed antibodies exhibit the claimed specificity. As can be seen, no such reasons have been presented here. *In re Marzocchi*, 169 USPQ 367 (CCPA, 1971).

Moreover, although it was not necessary to do so, applicants have shown in two declarations filed in ancestor application 08/412,227 (both of which are attached hereto for the convenience of the Examiner) that instantly claimed antibodies are, in fact, specific for p60 of *Listeria monocytogenes*. See, *e.g.*, the Declaration of Dr. Vormbrock, filed with the Response of March 3, 1997, which shows that antibodies generated against peptides of SEQ ID NO: 30 (as recited in instant claim 57) and SEQ ID NO: 42 (which is a form of SEQ ID NO: 20, as recited in instant claims 42 and 43) are specific for p60 of *L. monocytogenes*. See also the Declaration of Dr. Schubert, filed with the Preliminary Amendment of March 27, 1995, which shows that an antibody generated against the peptide of SEQ ID NO: 42 is specific for p60 of *L. monocytogenes*.

Further evidence to support applicants' contention that antibodies prepared according to the present invention react specifically with a 60 kD protein of the pathogenic bacterium, *L. monocytogenes*, is provided in the attached (post-filing) publication by a group which overlaps with the instant inventors (Bubert *et al.*, *Applied and Environmental Microbiology* 60, 3120-3127, 1994). (In Bubert, PepA corresponds to SEQ ID NO: 17 and PepD corresponds to SEQ ID NO: 20.) See, *e.g.*, the abstract; page 3122, second column and Figure 4, which show Western blot analysis; and page 3123, which shows an analysis by a sandwich ELISA assay. This publication is also discussed by Dr Blubert in the attached Declaration.

Supplementally, the attached Declaration by Dr. Blubert shows that an antibody produced by the method of the invention binds specifically to recombinant *E. coli* bacteria which produce the heterologous p60 protein from *Listeria monocytogenes*. Because *E. coli*, themselves, do not produce p60, this experiment further supports applicants' contention that the protein to which antibodies of the invention bind when they bind to *L. monocytogenes* is, in fact, the p60 protein produced by those listeria.

As can be seen, evidence of specificity is abundant. There is no contrary evidence.

The Examiner alleges that applicants have not taught how to screen for antibody specificity. Methods for determining the specificity of polyclonal or monoclonal antibodies, or screening for such antibodies, are conventional in the art. See, *e.g.*, the references listed in the specification at page 12, lines 11-16. Attached for the convenience of the Examiner is a chapter from one of those cited references (Harlow and Lane), which discloses in great detail how such procedures are carried out. See, *e.g.*, pages 148-173 for methods to produce monoclonal antibodies, and pages 174-179 for methods to screen them. A patent need not teach, and preferably omits, what is well known in the art. *Spectra-Physics, Inc. v. Coherent, Inc*, 3 USPQ2d 1737 (Fed. Cir. 1987).

The Examiner further alleges that applicants have failed to show that the instant antibodies, which were raised against peptides, react with intact p60. However, as was shown in detail above, the instant antibodies, all of which were raised against peptides, do, in fact, react with intact p60.

The rejection under 35 USC §112, second paragraph is unwarranted. Claim 43 is in product-by-process format, which is a perfectly acceptable form of claim recitation. See, *e.g.*, MPEP 2173.05(p) and 2113. Whether the process language carries "patentable weight" is irrelevant.

The "prior art made of record and not relied upon" has not been reviewed or commented upon by applicants. This is not to imply agreement or not with the comments of the Examiner.

The rejections should be withdrawn.

Respectfully submitted,

Anthony J. Zelano (Reg. No. 27,969)
Attorney for Applicants

Nancy J. Axelrod (Reg. No. 44,014)
Patent Agent
MILLEN, WHITE, ZELANO & BRANIGAN, P.C.
Arlington Courthouse Plaza I
2200 Clarendon Boulevard, Suite 1400
Arlington, Virginia 22201
(703) 243-6333

NJA/bgk
Filed: **June 11, 2001**
K:\Merck\1694d2\Reply, 6-8-01.wpd

MARKED-UP VERSION

42. (Amended) An isolated antibody which specifically binds to the p60 protein from pathogenic listeria, wherein said antibody binds an epitope from the peptide, SEQ ID NO: 17, 20, 26, 29, 30 or 31.

Since claims 59-62 are newly added, no marked-up version is necessary.